

REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

The Office Action Summary correctly indicates that claims 1-15 and 17-31 are pending in the application. Claims 4, 5, 7, 8, 15, and 17-30 have been withdrawn from consideration.

It is noted that the Office Action summary indicates that 1-3, 6, 9-14 and 31 have been rejected. However, only claims 1-3, 6 and 9-14 are indicated as rejected in the body of the Office Action.

Rejection under 35 U.S.C. § 103(a)

Claims 1-3, 6 and 9-14 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Goodman et al. (WO 98/27960) in view of Fleischer (1999, abstract only), or Fleischer (1999) and Miller et al. (1980, abstract only). This rejection is respectfully traversed.

The Office acknowledges that Goodman et al. fails to teach a method of treating atopic dermatitis. The Office asserts that a person of ordinary skill in the art would have been motivated to use the composition taught by Goodman et al. in the treatment of atopic dermatitis because allegedly Fleischer teaches that atopic dermatitis is a form of eczema and further that immune suppressants are used in the treatment of dermatitis. The Office alleges that Miller teaches that tinidazole is an effective immunosuppressant in vivo.

The rejection appears to result from an impermissible application of hindsight, picking and choosing from among a wide range of non-specific teachings in the field concerning dermatological treatments only those teachings which can be combined to arrive

at the allegations of the rejection and ascribing teachings to Fleischer that derive from the success of Applicants disclosed invention.

No evidence has been adduced from the cited references or the art that shows that anyone prior to the present inventors appreciated that the composition described in the present claims could be used in a method of treating atopic dermatitis as presently claimed. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990).

It is impermissible to first ascertain factually what [applicants] did and then view the prior art in such a manner as to select from the random facts of that art only those which may be modified and then utilized to reconstruct appellants' invention from such prior art. *In re Shuman*, 150 U.S.P.Q. 54, 57 (CCPA 1966); *Panduit Corp. v. Dennison Mfg. Co.*, 227 U.S.P.Q. 337, 343 (Fed. Cir. 1985). Such impermissible hindsight appears to have been applied in the making present rejection.

The treatment of atopic dermatitis has been very difficult and has not been regarded in the art as the same as or similar to the treatment of other skin diseases. There has been no effective treatment for atopic dermatitis despite many years of effort. Thus, the present invention of an effective method for the treatment of atopic dermatitis has been a strongly desired, but unmet need for many years. *See* page 1, line 20 to page 2, line 25 of the present application. Being such a strongly desired, but unmet need, the non-obvious nature of the invention is evidenced by the fact that the present inventors are the first to have created the claimed treatment method.

Moreover, the teachings of the secondary references would not have provided one or ordinary skill in the art with a motivation to modify Goodman et al. as proposed. Goodman

et al. discloses various diseases to be treated by their composition on page 1, lines 12 to 22.

However, Goodman et al. failed to appreciate that an antimicrobially active nitroimidazol drug, *i.e.*, nitroimidazol drug such as metroinidazole and tinidazole, would be effective for the treatment of atopic dermatitis.

Furthermore, the allegations of the Office concerning the secondary references miss their mark. For example, Fleischer teaches that “immune dysregulation appears to play an important role in the cause of atopic dermatitis,” not that immune regulation plays an important role as alleged by the Office. Fleischer teaches that topical corticosteroid agents have been the mainstay of therapy for atopic dermatitis because of their broad immunomodulatory effects. However, topical corticosteroid agents are not ideal agents because when used over the long term, they may cause cutaneous atrophy and immunosuppression. That is, Fleischer clearly indicates that immune dysregulation appears to play an important role in the cause of atopic dermatitis and therefore, it has been believed that topical corticosteroid agents having broad immunomodulatory effects are effective for the treatment of atopic dermatitis. Fleischer does not teach that immunosuppression is key to treating atopic dermatitis, indeed Fleischer appears to teach that immune suppression is a side effect of corticosteroids to be avoided.

Fleischer sought different effective agents for the treatment of atopic dermatitis and identified tacrolimus. Fleischer indicates that tacrolimus affects a broad spectrum of inflammatory mediators and processes known to be relevant to atopic dermatitis pathogenesis. Fleischer never suggests that any immunosuppressant can be an effective agent for the treatment of atopic dermatitis. Thus it appears that the Office has used impermissible hindsight to attach meaning to Fleischer that would not have been considered by one of ordinary skill in the art in the absence of the teachings of the present invention.

The combination of Miller with Fleischer and Goodman is no more successful in suggesting the modification of Goodman proposed by the Office. Miller teaches that two compounds, clotrimazole and dacarbaazine (DTIC) produced a dose related suppression of a tested response. . . . whereas metronidazol and tinidazole actually enhanced the response It is suggested that experiments of this kind are helpful in identifying those imidazol compounds that could be used as immunosuppressants in vivo. Thus, Miller teaches experiments that are proposed to be helpful in identifying whether imidazol compounds can be used as immunosuppressant in vivo. Miller does not teach that tinidazole can be used as an immunosuppressant in vivo or suggest the proposed modification of Goodman, even considering the teaching of Fleischman.

In view of the foregoing, the combination of references cited by the Office fails to teach or suggest the claimed invention. Thus, a proper *prima facie* case of obviousness has not been established.

Even if a *prima facie* case of obviousness could be made from the cited art, which has not been done, it is well recognized that secondary considerations, such as unexpected results and a long felt yet unmet need, can serve to rebut a *prima facie* case of obviousness.

As discussed above, the presently claimed method satisfies a long felt but unmet need. No effective treatment for atopic dermatitis was created prior to the present invention despite substantial efforts in the art. There is no evidence that any person prior to the present inventors appreciated the possibility of the presently claimed methods of treating atopic dermatitis. Further more, as has been pointed out, the specification of the present application provides evidence of unexpected superior effects in the treatment of atopic dermatitis which is nowhere appreciated in the prior art. For example, the present specification includes Test Examples 3 (pages 147-148), 4 (pages 148-150), 7 (pages 153-154), and 8 (pages 155-156)

wherein ointments or creams containing tinidazole were used to treat atopic dermatitis demonstrate that the present invention produces such unexpected superior effects.

For at least these reasons, the prior art would not have suggested the present invention to one of ordinary skill. Moreover, the unexpected superior results and the long felt but unmet need satisfied by the claimed invention serve to rebut any *prima facie* obviousness that could possibly be made. As such, withdrawal of this rejection is appropriate and is respectfully requested.

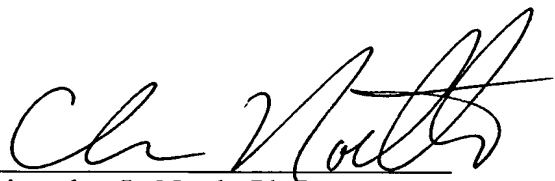
From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this Amendment and Reply or the application in general, the Examiner is respectfully requested to telephone the undersigned attorney so that prosecution of the application may be expedited.

Respectfully submitted,

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Date: November 2, 2005

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